Essential Needs and Current Gaps: Surveillance and Laboratory Support for Vaccine Development

Nancy J. Cox, Ph.D.
Director, Influenza Division
National Center for Immunization and Respiratory Diseases
Centers for Disease Control and Prevention

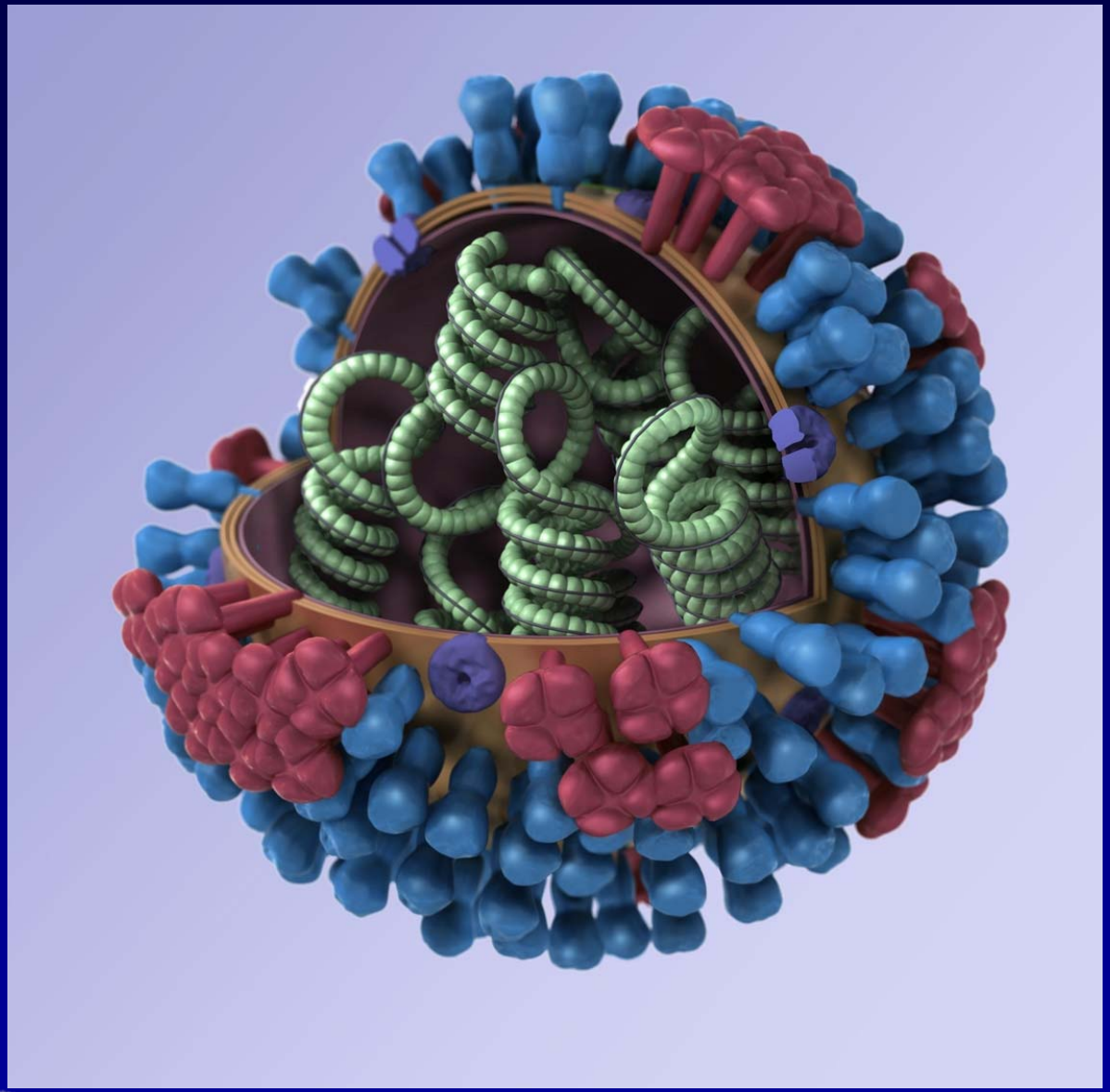
www.cdc.gov/H1N1flu

Presentation Themes

- Challenges for global influenza surveillance and capacity building
  - ✓ Need for funding and partnerships continues
  - ✓ More rapid detection of new pathogens
- Challenges for faster vaccine development/availability for pandemics
  - ✓ Better growing vaccine viruses (focused R&D)
  - ✓ Faster methods for making potency testing reagents
- Importance of partnerships & rapid virus and information sharing

Preparing for a Pandemic in the 21st Century

- H5N1 experience (and previous pandemics and epidemics) shaped expectations
  - Emergence in Asia, not North America
  - Origin in avian species, not swine
  - Planning for H5N1 dominated (greatest focus on 1918-like scenarios)
- Preparing global surveillance/diagnostic capability for a pandemic is challenging because……



The virus is the problem!

- 16 subtypes of HA and 9 of NA with constant evolution and reassortment of genes
- Most dx tests do not differentiate subtypes
- Need for rapid tests for AV resistance and immunity

Increasing Detections of Human Infections by Swine Influenza Viruses

Shinde, NEJM 2009

- Improved dx testing at state level (5 target rRT-PCR)
- Novel influenza virus infections of humans made notifiable
  - ✓ Increasing numbers of swine influenza cases detected over past five years – *Shinde, NEJM 2009*
- Increasing efforts at states, CDC, and USDA to identify and investigate human cases of swine influenza
- Apparent limited secondary transmission but detections and virus characterization lead to increased awareness in states and better laboratory preparedness at CDC

Timeline for Testing First Clinical Samples

- April 15 – First specimen arrived at CDC; test + for swine influenza NP and weakly + for H1sw HA-> seq
- April 17 - Second specimen arrives; partial sequences analyzed for 8 gene segments indicate unique gene combination; genes closest to those of influenza viruses previously detected in swine in N America and Eurasia (new reassortant)
- April 18 – Seq all 8 gene segments of A/CA/4/09; decision to clean GLP lab to prepare rg vax candidate
- April 23 – A/CA/5/09 and A/CA/5/09 tested in HI test; antigenically related to swine triple reassortant H1 viruses; Mexican samples tested - similar to CA viruses
- April 24 – Total genome seqs for 4 viruses from 3 patients (CA and TX); total of 8 US cases

CDC Distribution of Influenza Diagnostic/Surveillance Kits

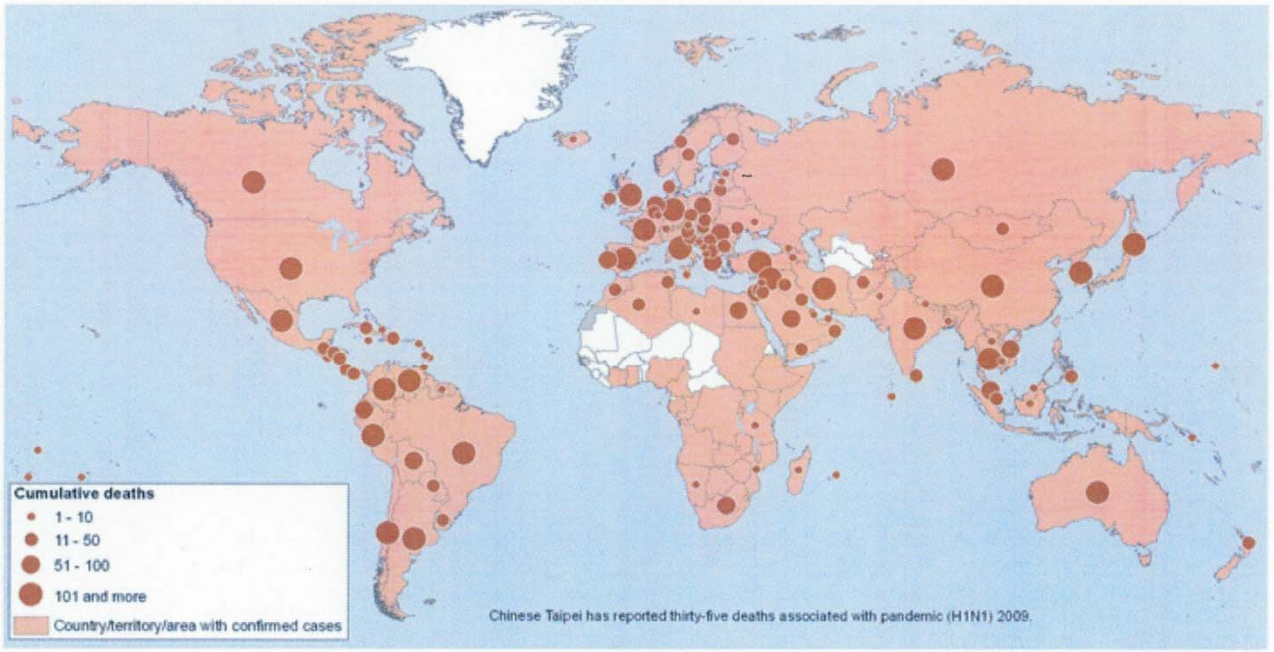
- Development of proficiency testing panels and programs is work in progress
- 2,000 rRT-PCR kits distributed globally
  - ✓ 312 international labs in 153 countries
  - ✓ 144 kits in 50 states DC and PR
  - ✓ Resulted in receipt by CDC's WHO CC of many "unsubtypable" samples
- Over 200 WHO reference kits with antigens and antisera distributed globally
  - ✓ 140 international kits
  - ✓ 119 domestic kits

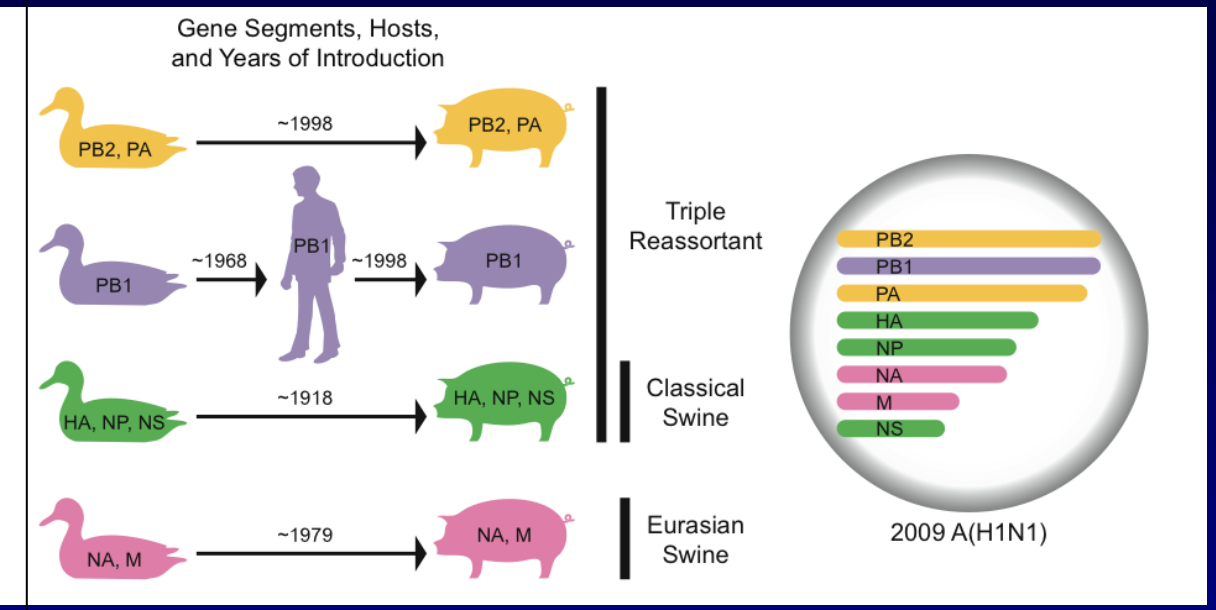
World Health Organization

Timeline (22 July 2009 onwards)
Pandemic (H1N1) 2009 laboratory confirmed cases
And number of deaths as reported to WHO

Status as of: 03 January 2010

Previous





First cases in Mexico: 24 February

April 15	April 29	May 3	May 23
First case Identified A/California/4/2009	First Diagnostic Kits Shipped to State Labs	First Diagnostic Kits Shipped to WHO Network	Vaccine Strain Shipped to Manufacturers

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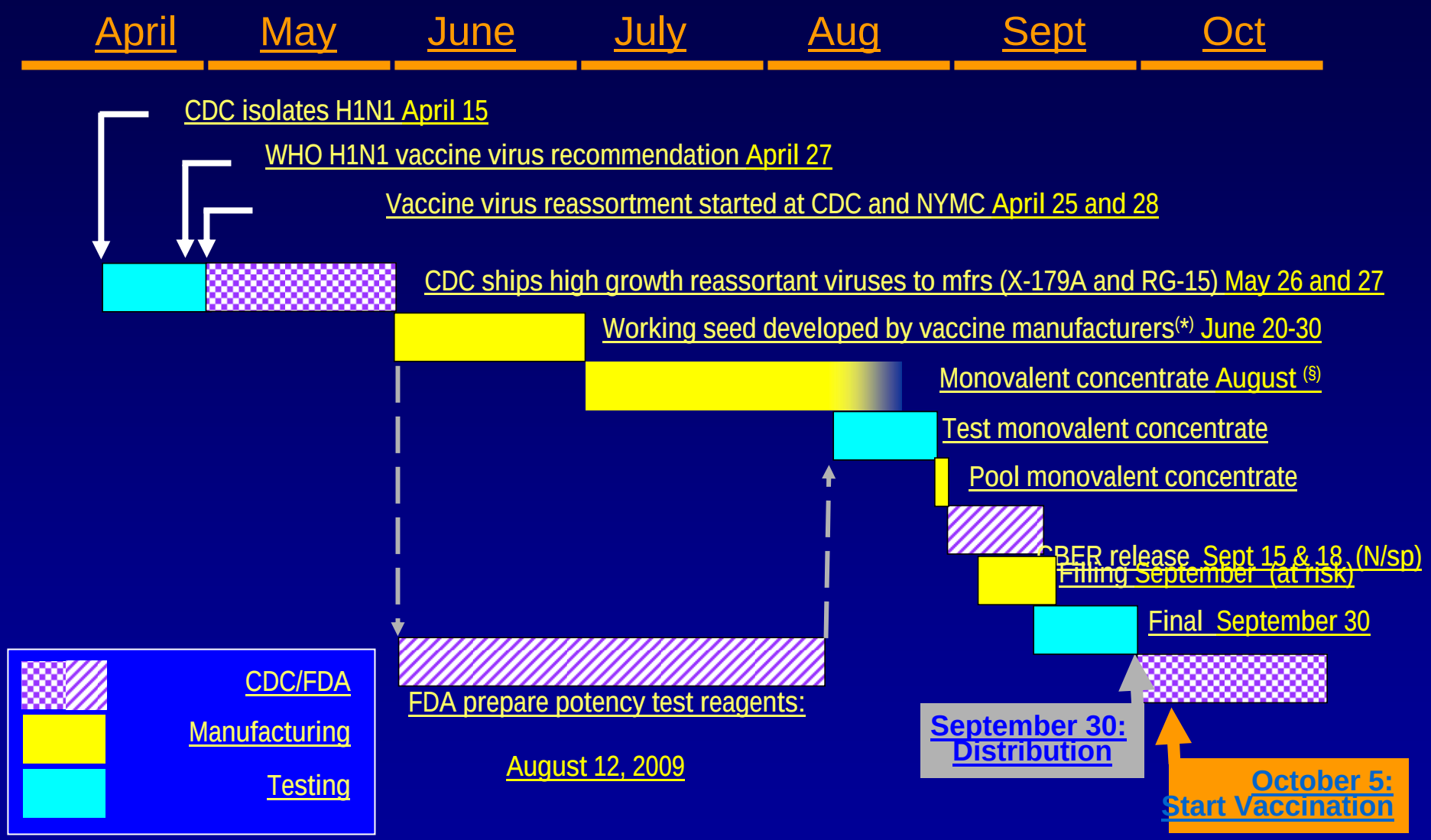
Estimated Timeline of H1N1pdm Vaccine Development and Delivery in the U.S.



(*) Manufacturers were transiently limited in their ability to develop seed viruses due to lack of facilities to grow virus in large volume at the required BSL3 biocontainment

(§) Production of monovalent inactivated vaccine is a continuous process

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The H1N1 Response Went Well

- We were better prepared and lucky
  - ✓ Much better prepared due to H5N1 preparedness
  - ✓ Dx preparedness due to swine influenza infections in humans in the US
  - ✓ Funding to produce and distribute tests (rRT-PCR) globally
  - ✓ Sharing of viruses and information accelerated vaccine development
  - ✓ H1N1 vaccine very immunogenic and viruses homogeneous
  - ✓ Disease mild relative to Asian and Spanish flu pandemics
  - ✓ Vaccine adverse events surveillance has not picked up signals

Incremental Improvements That Could Change the Game Next Time: Two Small Steps

Move recognition of the outbreak 2 weeks to 1 month earlier (9 April) through better diagnostic/surveillance preparedness

→ Save two weeks/1month in availability of influenza vaccines

→ More countries can identify and subtype influenza viruses and are aware that un-subtypable viruses raise a red flag for investigation

More rapid vaccine production; move just 2 weeks earlier through developing better growing vaccine viruses and streamlining production of potency testing reagents

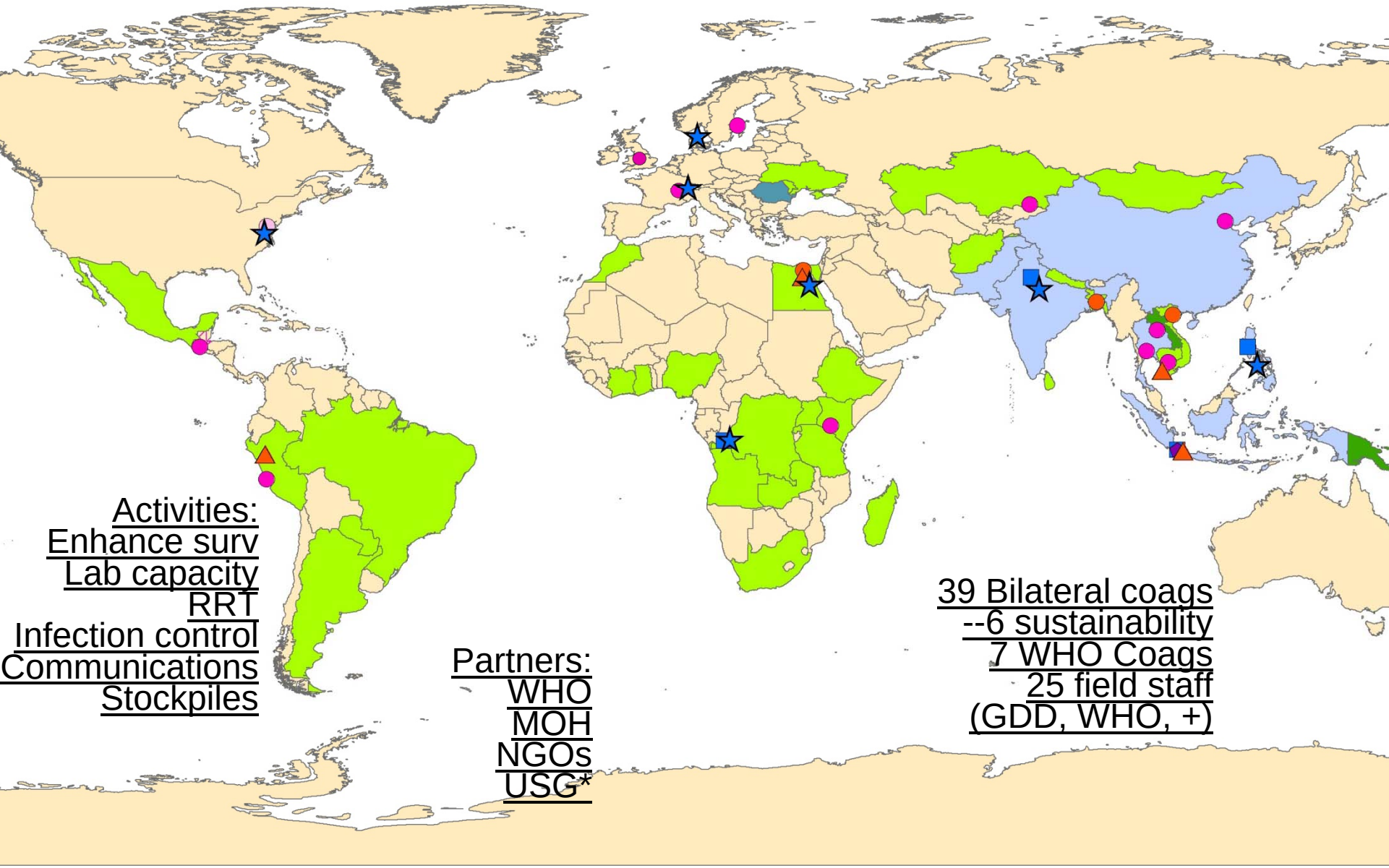
→
- Make more candidate vaccine viruses available; ID molecular determinants for high virus yield in eggs and cells and improve yield
- Focus on novel ways to quantitate antigens in older and new vaxs

AI/PI Preparedness: Technical Package

- Enhance international capacity for surv of influenza
- Decrease time to detect, report & respond to cases
  - ✓Use M&E tool for assessing progress
- Enhance health systems preparedness
- Evidence base for vaccine introductions
  - ✓Implement vaccine policy where appropriate
  - ✓**Decrease the burden of influenza**

•One Health Approach
•Whole of Society Approach
•Health Systems Enhancements
•Assist with vaccine production/planning

2009 Influenza Cooperative Agreements



Lessons Learned from the H1N1 Pandemic

- Global preparedness for a possible H5N1 pandemic made response to the H1N1 pdm much easier
- Well-developed global networks (e.g, GISN), relationships and partnerships allowed for a more coordinated and measured global response
- Rapid information & virus sharing essential for an effective pandemic response; must preserve rapid sharing for development of dx tests and vaccines
- Better surveillance for influenza in domesticated animals - essential for pandemic preparedness
- H1N1 pandemic reinforced understanding of the “two-way street” involving exchange of influenza viruses between humans & domestic/companion animals – MUCH more to do to improve surveillance at AHI

Lessons Learned from the H1N1 Pandemic

- Having influenza vaccines 1 month earlier likely to make big difference in disease reduction and vaccine acceptance

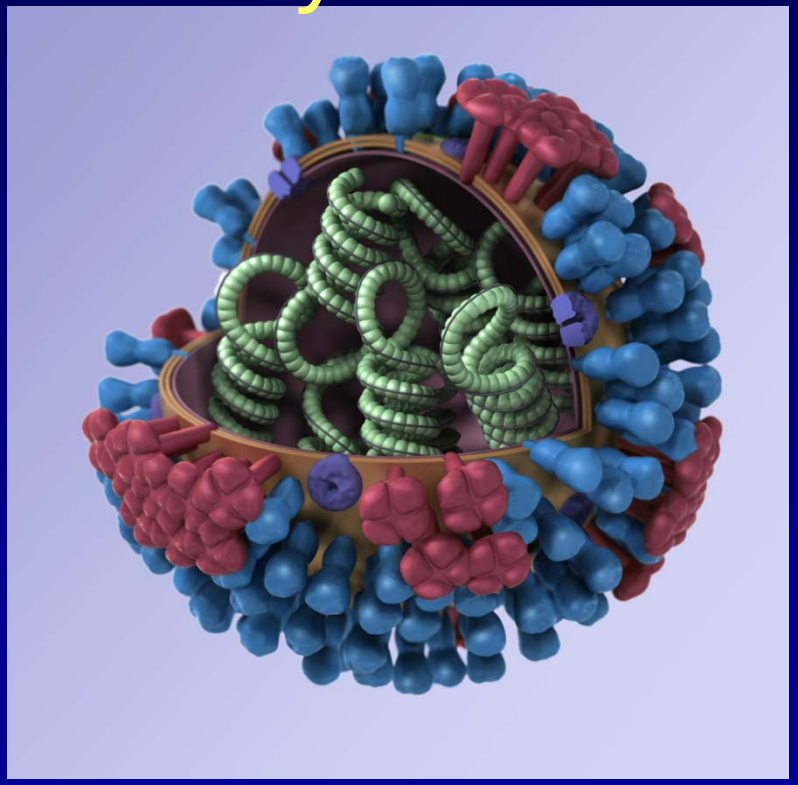
  ✓THE FUTURE

- Set goal: Move detection of novel influenza viruses closer to emergence & the availability of vax closer to disease occurrence
  - ✓ Need funding for sustainable global flu surveillance
  - ✓ Need to continue surveillance and vaccine capacity building in all WHO regions, esp. AFRO and EMRO
  - ✓ Expand rRT-PCR for tests for flu/respiratory diseases
  - ✓ Develop better POC dx tests and rapid immunity tests
  - ✓ Need better signal to noise filters for respiratory disease
  - ✓ Streamline methods for measuring vax Ag content

Acknowledgements

- State and Local Health Departments and DoD Laboratories
- Other PH Colleagues Around the World
- Other USG Departments/Agencies
- Colleagues in Veterinary Health
- WHO's Global Influenza Surveillance Network +
  - ✓ National Influenza Centers (esp. Mexico and Canada's NICs)
  - ✓ WHO CCs
  - ✓ WHO RO and HQ
- Influenza Division Staff, CDC
  - ✓ Office of the Director
    - ✓ Carolyn B. Bridges, Associate Director for Science
    - ✓ **Dan Jernigan, Deputy Director**
    - ✓ Michael Shaw, Associate Director for Laboratory Science
  - ✓ Epidemiology and Surveillance Branch
    - ✓ Joe Bresee, Chief
  - ✓ Immunology and Pathogenesis Branch
    - ✓ Jackie Katz, Chief
  - ✓ Viral Surveillance and Diagnostics Branch
    - ✓ Alexander "Sasha" Klimov, Chief
  - ✓ Molecular Genetics Branch
    - ✓ Ruben Donis, Chief

We have a new “player” in the flu field- H1N1pdm ; don’t forget H2N?, H5N1,H7N?, H9N2…..The next pandemic may not wait 40 years.



Thank you!

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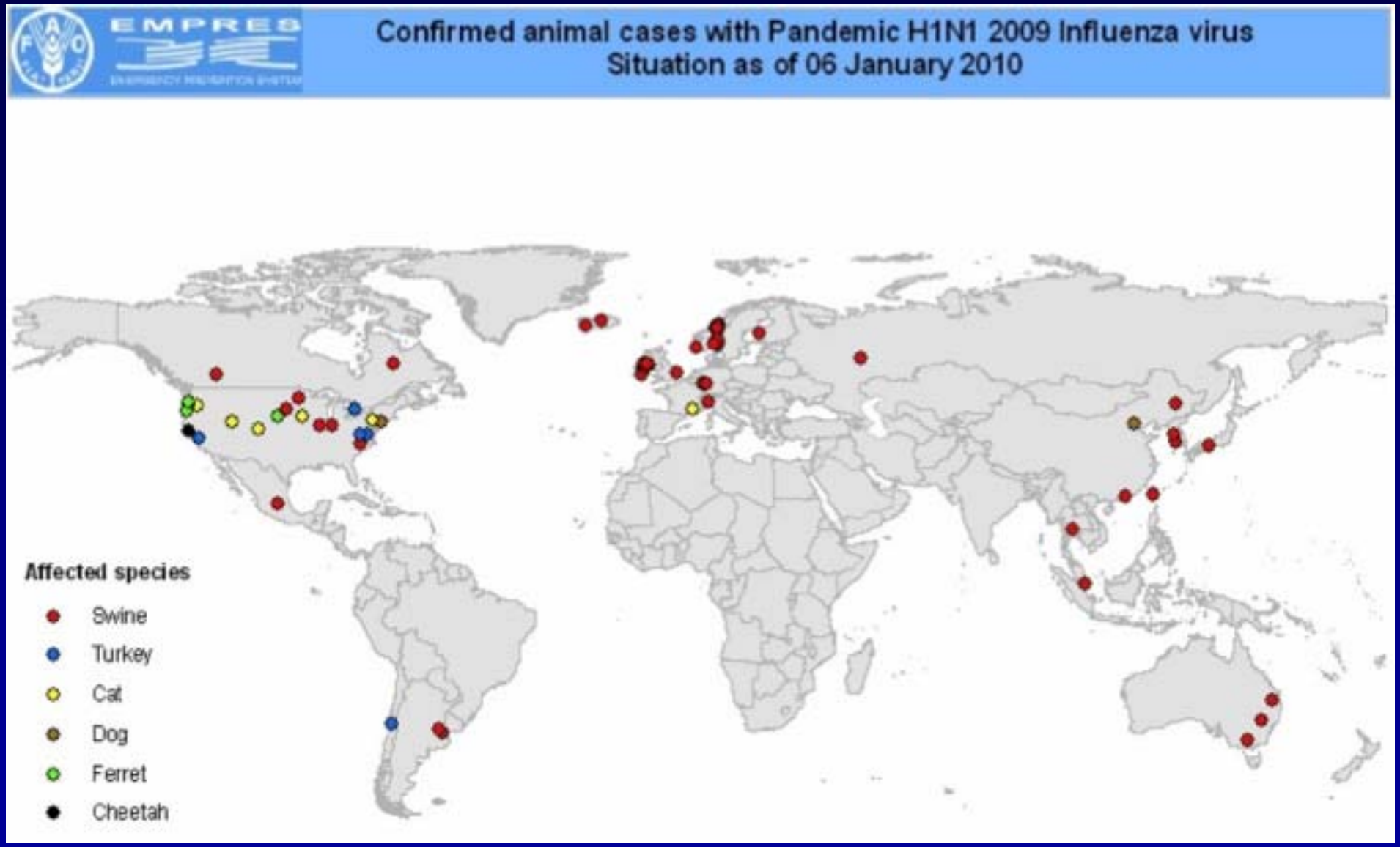
EMPRES
Confirmed animal cases with Pandemic H1N1 2009 Influenza virus
Situation as of 06 January 2010
Affected species
Swine
Turkey
Cat
Dog
Ferret
Cheetah